REMARKS

Claims 6-11, 20-28, 31-33, 39-43, 49-53, 55, 57, 60, 61, 64, 65, and 72-77 are pending in the application. Claims 6-11, 20-23, 28, 31-33, and 43 have been amended. Claims 1-5, 12-19, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, 63, and 66-71 have been cancelled without prejudice. New claims 72-77 have been added. Support for the amendments and new claims can be found in the specification at, e.g., page 24, line 8, to page 25, line 5. No new matter has been added.

Claim Objections

At page 3 of the Office Action, claims 18 and 29 were objected to as containing typographical errors. These claims have been cancelled without prejudice, thereby rendering their objection moot.

35 U.S.C. § 101

At page 3 of the Office Action, claims 1-3, 5-9, and 11 were rejected as allegedly directed to non-statutory subject matter.

Claims 1-3 and 5 have been cancelled without prejudice, thereby rendering their rejection moot.

Claims 6 and 7 have been rewritten as independent claims to include the term "isolated" and thereby overcome the rejection. Claims 8, 9, and 11 depend from claim 7.

In view of the amendments and claim cancellations, applicants request that the Examiner withdraw the rejection.

35 U.S.C § 112, 2nd Paragraph (Indefiniteness)

At pages 3-4 of the Office Action, claims 4 and 10 were rejected as allegedly indefinite in their recitation of the phrase "comprising an antibody that is a monoclonal antibody."

Claim 4 has been cancelled without prejudice, thereby rendering its rejection moot.

Claim 10 has been amended to recite the phrase "wherein the antibody or fragment thereof is a monoclonal antibody."

In view of the amendment and claim cancellation, applicants request that the Examiner withdraw the rejection.

35 U.S.C. § 112, 1st Paragraph (Enablement)

At pages 4-7 of the Office Action, claims 1-5, 9, 12-19, 23, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63 were rejected as allegedly not enabled.

Claims 1-5, 12-19, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63 have been cancelled, thereby rendering their rejection moot.

Dependent claims 9 and 23 limit claims 7 and 21 by requiring that the claimed antibody or fragment thereof be an F(v) fragment, a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, or a dimer consisting of one heavy and one light chain.

In rejecting claims 9 and 23, the Office Action asserted that

> the lack of guidance, lack of sufficient working examples, and the amount of experimentation required does not enable one skilled in the art to make and use antibody fragments consisting of a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain that specifically bind to a low density lipoprotein binding protein-2 (LBP-2).

The Office Action cited Hollinger et al. (2005) Nature Biotechnology 9:1126-36 ("Hollinger") in support of the assertions that "single chain variable domain antibodies rarely retain the affinity of the parent antibody and are also poorly soluble and often prone to aggregation..." and "to form dimers and trimers, the length of the linker region is important and that the length of linkers affects stability."

Applicants respectfully submit that the person of ordinary skill in the art at the time the present application was filed would have been able to make and use the antibodies and antibody fragments of claims 9 and 23 without undue experimentation and with a reasonable expectation of success.

Hollinger reviews single variable domain antibodies and contains citations to several references that describe the use of this technology (see Hollinger at pages 1127-28). Despite

certain noted drawbacks of single variable domain antibodies (as compared to their parent antibodies), there is nothing in Hollinger to indicate that it would require undue experimentation to make and/or use such antibodies. The assertion that single variable domain antibodies may have deficiencies as compared to their parent antibodies (e.g., reduced affinity) certainly does not preclude one from making and using them. Satisfaction of the enablement requirement requires only that the skilled person be able to make and use the claimed antibodies without undue experimentation and with a reasonable expectation of success, not that the antibodies retain all features and advantages of the parent antibodies from which they are derived. Hollinger confirms that single variable domain antibodies were well known known in the art at the time the present application was filed.

In addition to single variable domain antibodies, Hollinger also describes (on pages 1128-30) several multivalent designs for antibodies. Rather then negating the patentability of claims 9 and 23, Hollinger confirms the art's familiarity with the preparation and use of dimeric and trimeric antibodies. With respect to the Office Action's comments regarding a linker region, the preparation of a linker region having an appropriate length for a given antibody requires only routine experimentation and is well within the skill of an ordinary biologist. See, e.g., *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988) in which the court found that screening many hybridomas to find the few hybridomas that fell within the claims did not require undue experimentation. The description in Hollinger of many different multivalent designs of antibodies confirms the enablement of claims 9 and 23 as directed to dimeric and trimeric forms of antibodies.

The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known and already available to the public. MPEP § 2164.05(a). Furthermore, the specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without undue experimentation. MPEP § 2164.02. Because the antibodies and antibody fragments of claims 9 and 23 were well known in the art at the time of filing of the present application, it would have required no undue experimentation for the skilled person to

apply well known technologies to prepare such antibodies and antibody fragments directed against the LBP-2 polypeptides recited in the claims.

In view of the claim amendments and the foregoing comments, applicants request that the Examiner withdraw the rejection.

35 U.S.C. § 112, 1st Paragraph (Written Description)

At pages 7-10 of the Office Action, claims 1-5, 9, 12-19, 23, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63 were rejected as allegedly not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 1-5, 12-19, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63 have been cancelled, thereby rendering their rejection moot.

As detailed above, dependent claims 9 and 23 limit claims 7 and 21 by requiring that the claimed antibody or fragment thereof be an F(v) fragment, a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, or a dimer consisting of one heavy and one light chain.

The antibodies and antibody fragments recited in claims 9 and 23 are described in the specification at, e.g., page 24, lines 11-15. As detailed above in response to the enablement rejection, these antibodies and antibody fragments were well known in the art at the time the present application was filed. As a result, the skilled person would have readily understood the meaning of the antibody and antibody fragment terms recited in the claims and would have understood applicants to have invented the anti-LBP-2 antibodies and antibody fragments and have been in possession of the claimed subject matter at the time of filing of the application.

In view of the claim amendments and the foregoing comments, applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance.

Enclosed is a Petition for Three Month Extension of Time and a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 10797-004005.

Respectfully submitted,

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